

CLAIMS

What is claimed is:

- 5 1. An isolated polynucleotide encoding a fusion protein formed between a human serum albumin (HSA) and a cell proliferation stimulatory factor (CPSF), comprising:
a first nucleotide sequence at least 90% identical to SEQ ID NO. 11 and a second nucleotide sequence encoding a (CPSF) positioned either 5'- or 3'- to the first
10 nucleotide sequence, wherein the first and second nucleotide sequences are operably linked to be expressed as a fusion protein of HSA and CPSF.
- 15 2. The isolated polynucleotide of claim 1, wherein the first nucleotide sequence is at least 95% identical to SEQ ID NO. 11.
3. The isolated polynucleotide of claim 1, wherein the first nucleotide encodes an amino acid sequence comprising SEQ ID NO. 12.
- 20 4. The isolated polynucleotide of claim 1, wherein the second nucleotide sequence is at least 90% identical to SEQ ID NOS. 13, 15, 17, 19, or 21.
5. The isolated polynucleotide of claim 1, wherein the second nucleotide encodes an amino acid sequence comprising SEQ ID NOS. 14, 16, 18, 20, or 22.
- 25 6. The isolated polynucleotide of claim 1, wherein the CPSF is selected from the group consisting of G-CSF, GM-CSF, (EOS)-CSF, CSF-1, EPO, IL-1; IL-2, IL-3, IL-4; IL-6; IL-7; IL-8, IL-9; IL-10; IL-11; IL-12; IL-13, IL-18, SLF, SCF, mast cell growth factor, EPA, Lactoferrin, H-subunit ferritin, prostaglandin (PG) E1 and E2, TNF- α , TNF- β , IFN- α -1b, IFN- α -2a, IFN- α -2b, IFN- β , IFN- ω , IFN- γ ; TGF- β , activin, inhibin, leukemic inhibitory factor, oncostatin M, MIP-1- α ,

MIP-1 β ; MIP-2- α , GRO- α ; MIP-2- β , platelet factor-4, macrophage chemotactic and activating factor and IP-10.

7. The isolated polynucleotide of claim 1, further comprising a third nucleotide sequence encoding a peptide linker that links the HSA and the CPSF.
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8. The isolated polynucleotide of claim 7, wherein the peptide linker is a (G₄S)₃₋₄ linker.
- 10 9. The isolated polynucleotide of claim 7, wherein the length of the peptide linker is 2-100 aa.
10. The isolated polynucleotide of claim 7, wherein the length of the peptide linker is 5-50 aa.
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11. The isolated polynucleotide of claim 7, wherein the length of the peptide linker is 14-30 aa.
12. An isolated polynucleotide, comprising:
20 a nucleotide sequence at least 90% identical to SEQ ID NO. 1.
13. The isolated polynucleotide of claim 12, wherein the nucleotide sequence is at least 95% identical to SEQ ID NO. 1.
- 25 14. The isolated polynucleotide of claim 12, wherein the nucleotide sequence encodes an amino acid sequence comprising SEQ ID NO. 2.
15. An isolated polynucleotide, comprising:
a nucleotide sequence at least 90% identical to SEQ ID NO. 3.
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16. The isolated polynucleotide of claim 15, wherein the nucleotide sequence is at least 95% identical to SEQ ID NO. 3.
17. The isolated polynucleotide of claim 15, wherein the nucleotide sequence encodes 5 an amino acid sequence comprising SEQ ID NO. 4.
18. An isolated polynucleotide, comprising:
a nucleotide sequence at least 90% identical to SEQ ID NO. 5.
- 10 19. The isolated polynucleotide of claim 18, wherein the nucleotide sequence is at least 95% identical to SEQ ID NO. 5.
20. The isolated polynucleotide of claim 18, wherein the nucleotide sequence encodes an amino acid sequence comprising SEQ ID NO. 6.
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21. An isolated polynucleotide, comprising:
a nucleotide sequence at least 90% identical to SEQ ID NO. 7.
22. The isolated polynucleotide of claim 21, wherein the nucleotide sequence is at 20 least 95% identical to SEQ ID NO. 7.
23. The isolated polynucleotide of claim 21, wherein the nucleotide sequence encodes an amino acid sequence comprising SEQ ID NO. 8.
- 25 24. An isolated polynucleotide, comprising:
a nucleotide sequence at least 90% identical to SEQ ID NO. 9.
25. The isolated polynucleotide of claim 24, wherein the nucleotide sequence is at least 95% identical to SEQ ID NO. 9.
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26. The isolated polynucleotide of claim 24, wherein the nucleotide sequence encodes an amino acid sequence comprising SEQ ID NO. 10.
27. The isolated polynucleotide of any of claims 1, 12, 15, 18, 21 and 24, wherein the protein encoded by the polynucleotide binds to a specific antibody of human albumin.
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28. A recombinant vector, comprising:
the sequence of the polynucleotide in claims 1, 12, 15, 18, 21 and 24.
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29. The recombinant vector of claim 28, wherein the vector is an expression vector for expressing the fusion protein in a host organism selected from the group consisting of mammal, fish, insect, plant, yeast, and bacterium.
- 15 30. The recombinant vector of claim 29, wherein the host organism is yeast.
31. The recombinant vector of claim 30, wherein the strain of the yeast is selected from the group consisting of, but not limited, *Saccharomyces*, *Candida*, *Pichia*, *Kluyveromyces*, *Torulaspora*, or *Schinosaccharomyces*.
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32. The recombinant vector of claim 30, wherein the strain of the yeast.
33. The recombinant vector of claim 30, wherein the recombinant vector is a yeast transfer vector, such as pPICZ A, pPICZ B, or pPICZ C.
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34. A recombinant protein having an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 4, 6, 8, and 10.
35. The recombinant protein of claim 34, wherein the protein is recombinantly produced in yeast cells and glycosylated to substantially the same extent as that when recombinantly produced in mammalian cells.
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36. The recombinant protein of claim 35, wherein the mammalian cells are CHO cells.
- 5 37. The recombinant protein of claim 35, wherein the yeast cells are Pichia pastoris cells.
38. The recombinant protein of claim 28, wherein the protein has a shelf-life at least 5 times longer than that of the CPSF alone when stored under the same condition.
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39. The recombinant protein of claim 28, wherein the protein has a plasma half-life at least 3 times longer than that of the CPSF alone when administered in vivo.
40. A recombinant cell containing the recombinant vector of claim 28.
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41. The recombinant cell of claim 38, wherein the cell is selected from the group consisting of mammalian, fish, insect, plant, yeast, and bacterial cells.
42. A composition, comprising:
20 a combination of at least two different HAS/CPSF fusion proteins.
43. The composition of claim 42, wherein the combination is HSA/IL-11 fusion and HSA/EPO fusion.
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44. The composition of claim 42, wherein the combination is HSA/IL-3 fusion and HSA/EPO fusion.
45. The composition of claim 42, wherein the combination is HSA/IL-3 fusion and HSA/GCSF fusion.
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46. A method for treating a patient with a CPSF in need thereof, comprising:

administering a pharmaceutical formulation comprising a fusion protein of HSA and CPSF to the patient in a therapeutically effective amount.

47. A method for treating a patient with a hematological disorder, comprising:
5 administering a first pharmaceutical formulation comprising a first fusion protein of HSA and a first CPSF to the patient in a therapeutically effective amount; and administering to the patient a second pharmaceutical formulation comprising a second fusion protein of HSA and a second CPSF to the patient in a therapeutically effective amount.

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48. A method for treating a patient with a hematological disorder, comprising:
administering the composition of claim 42 to the patient in a therapeutically effective amount.

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49. A kit, comprising:
a first fusion protein of HSA and a first CPSF, and a second fusion protein of HSA and a second CPSF.

50. The kit of claim 49, wherein the first and second CPSF are different.

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